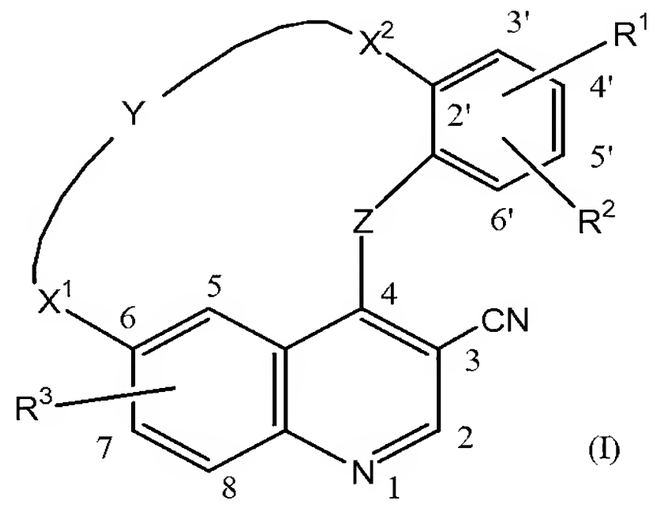
ABSTRACT

3-CYANO-QUINOLINE DERIVATIVES WITH ANTIPROLIFERATIVE ACTIVITY

The present invention concerns the compounds of formula



(I)

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

Z represents NH;

Y represents -C_{3-9}alkyl-, -C_{1-5}alkyl-NR^{12}-C_{1-5}alkyl-, -C_{1-6}alkyl-NH-CO- or -CO-NH -C_{1-6}alkyl- ;

X^1 represents -O-;

X^2 represents a direct bond, -NR^{11}-C_{1-2}alkyl-, -NR^{11}-CH_2-, -C_{1-2}alkyl-, -O-C_{1-2}alkyl, -O- or –O-CH_2-;

R^1 represents hydrogen or halo;

R^2 represents hydrogen, cyano, halo, hydroxycarbonyl-, C_{1-4}alkyloxycarbonyl-, Het^{16}-carbonyl- or Ar^5;

R^3 represents hydrogen, hydroxy, C_{1-4}alkyloxy-, Ar^4-C_{1-4}alkyloxy or R^3 represents C_{1-4}alkyloxy substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy- or Het^2-;

R^{10} represents hydrogen;

R^{11} represents hydrogen, C_{1-4}alkyl- or C_{1-4}alkyl-oxy-carbonyl-;

R^{12} represents Het^{14}-C_{1-4}alkyl, in particular morpholinyl-C_{1-4}alkyl;

Het^2 represents a heterocycle selected from morpholinyl or piperidinyl optionally substituted with C_{1-4}alkyl-, preferably methyl;

Het^{14} represents morpholinyl;

Het^{16} represents a heterocycle selected from morpholinyl or pyrrolidinyl;

Ar^4 represents phenyl;

Ar^5 represents phenyl optionally substituted with cyano.